REMARKS

I. Status of Claims

Claims 17-22, 24-28, and 30 are pending in the present application. Claims 26-27, and 30 are allowed. Claims 24 and 28 have been amended. Claims 17-19, 21-22, and 24-25, are rejected, and claim 20 is objected to. Claim 29 is withdrawn.

Support for the amendments to claims 24 and 28 may be found throughout the specification and claims as originally filed.

II. Objection to Specification

The specification is objected to for allegedly failing to provide proper antecedent basis for the claimed subject matter. Specifically the Office alleges that the limitation "a carrier comprising polyglycolic acids or polyglycolic acids" in claims 17 and 26 lacks clear support or antecedent basis in the specification.

Applicants respectfully traverse the objection and its supporting remarks. The specification on page 3, lines 8-15, indicates that carriers can be organic, inorganic, or both and further that the carrier can include (i.e., comprise) among other components "polylactic acids, polyglycolic acids, ..." Thus, there is antecedent support for the second carrier as claimed.

Applicants respectfully request that this objection to the specification be withdrawn.

III. Interpretation of Claims 24 and 28

Applicants acknowledge the Office's claim interpretation of claims 24 and 28 and agree that as amended, the polylactic acids or polyglycolic acids are not conjugated to the first antigen.

IV. Rejection under 35 U.S.C. § 112, First Paragraph (New Matter)

Claims 24 and 28 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, has possession of the claimed invention.

Applicants respectfully traverse the rejection and its supporting remarks. The Office has acknowledged that claims 24 and 28 contemplate that the polylactic acids or polyglycolic acids as "within a generic carrier, which encompasses organic carrier, inorganic carrier, cellular carrier, bacterial carrier, etc." However, the Office has asserted that there is no support for such a limitation in the as filed specification. Applicants respectfully disagree as the specification on page 3, lines 8-15, indicates that carriers can be organic, inorganic, or both and further that the carrier can include (i.e., comprise) among other components "polylactic acids, polyglycolic acids, ..." Furthermore, the carrier can also function as, and therefore include, an immunostimulatory agent which can include an adjuvant such as MF59. Applicants have clarified claims 24 and 28 so that it is clear that there is not a "third carrier", but rather that there is a second carrier that comprises MF59 and the polylactic acids or polyglycolic acids.

Applicants respectfully request that the rejection under 35 U.S.C. § 112, first paragraph, be withdrawn.

V. Rejections under 35 U.S.C. § 103(a)

Claims 17-19, 22 and 25

Claims 17-19, 22 and 25 are rejected under § 103(a) as allegedly being unpatentable over Granoff *et al.* (*infect. Immun.* 65: 1710-1715, May 1997, of record) (Granoff *et al.*, 1997) in view of Granoff *et al.* (*J. Pediatr.* 121: 187-194, 1992) (Granoff *et al.*, 1992), Vella *et al.* (*Biotechnology* 20: 1-22, 1992) and Frasch (*In*: *Development and Clinical Uses of Haemophilus B conjugate Vaccines*. (Ed) Willis *et al.* M. Dekker, New York, pages 435-453, 1994).

To the extent the rejection is applicable to the amended claims, Applicants respectfully traverse the rejection and its supporting remarks.

The Office has not established a *prima facie* case of obviousness. The Examiner has acknowledge that Granoff *et al.*, 1997 does teach the presence of outer membrane vesicles from serogroup B *Neisseria meningitidis* in their immunogenic vaccine composition. Therefore Granoff *et al.* 1997, provides no information as to the interaction between MF59 and NmB OMVs. Similarly, Granoff *et al.*, 1992, does not teach the presence of MF59 in their immunogenic vaccine compositions. Therefore, Granoff *et al.*, 1992, also fails to provide any information regarding the interaction between MF59 and NmB OMVs. MPEP § 2143 states that "combining known prior art elements is not sufficient to render the claimed invention obvious if the results would not have been predictable to one of ordinary skill in the art." One of skill in the art could not predictably combine Granoff *et al.*, 1997 with Granoff *et al.*, 1992 to produce the instant invention as neither provide any indication of how MF59 and NmB OMVs interact with one another.

In order to establish a *prima facie* case of obviousness, the Examiner must provide at least a reason that one of skill in the art would combine the cited references. The Examiner's assertion that "[o]ne of ordinary skill in the art would have been motivated to produce the instant invention for the expected benefit of providing a combination conjugate vaccine that includes a Hib conjugate that is more immunogenic than a conjugate comprising Hib oligomers conjugated to CRM197 after one or two doses and that advantageously elicits earlier acquisition of serum antibody than the conjugate comprising Hib oligomers ..." However, without knowing how MF59 and MenB OMVs interaction, one of skill in the art would not necessarily expect to achieve the benefits of the PRP-OMP conjugate. Indeed the instant specification in Table 3 demonstrates that changing from alum to MF59 in the NmC conj. + NmB vaccines actually ***decreases*** the immune response to the NmB OMVs. Thus, at least in the context of the NMC conj. + NmB OMVs, MF59 appears to have a deleterious effect upon the NmB OMV's immunogenicity (though still sufficient for the inventors' purpose hereunder). Thus, one of skill in the art would not be motivated to combine PRP-OMP with NmC oligosaccharide and MF59, given the general unpredictability of combining different adjuvants.

For at least the reasons set forth above, Applicants assert that claims 17-19, 22 and 25 would not be obvious in view of Granoff *et al.*, 1997, Granoff *et al.*, 1992, Vella *et al.*, and Frasch. Therefore, Applicants respectfully request that the rejection under 35 U.S.C. § 103(a) be withdrawn.

Claims 18 and 19

The rational provided by the Examiner applies even to a lesser extent to claims 18 and 19 which require that the capsular oligosaccharide from serogroup C *N. meningitidis* (NmC) is conjugated to a protein carrier. The Office has asserted that one of ordinary skill in the art would have been motivated to produce the instant invention for the expected benefit of providing "a combination conjugate vaccine that includes a Hib conjugate that is more immunogenic that a conjugate comprising Hib oligomers conjugated to CRM_{197}," (page 7 of the Office action mailed on 04/20/2009). However, the Office has not demonstrated why one of skill in the art would not also conjugate NmC to OMV for the expected benefit of increasing immunogenicity. Granoff *et al.*, 1992 teach that the Hib-NmB conjugate results in a higher immune response after a single injection compared to the Hib-CRM_{197} conjugate. Thus, the apparent benefit is fewer injections with the Hib-NmB conjugate. However, if one of skill in the art were to combine NmC-CRM_{197} with the Hib-NmB conjugate, the combination would most likely not result in a sufficiently immunogenic response to the capsular oligosaccharide from serogroup C *N. meningitidis* (NmC) conjugated to the protein carrier after a single injection, because Fig. 1 of Granoff *et al.*, 1992 indicates that three injections were required for a CRM_{197} conjugate to give a strong immune response. Thus, there would be no reasonable expectation of success in combining NmC-CRM_{197} with Hib-OMV and MF59 to obtain the benefits of a strong immune response to both capsular polysaccharides after a single injection. Even if one of skill in the art were motivated to replace the Hib-CRM_{197} with Hib-OMV, one of skill in the art would likely also replace the NmC-CRM_{197} with NmC-OMV in order to obtain the presumed benefits of conjugating the capsular polysaccharides to the OMV. Claims 18 and 19 would not read upon such a modified vaccine composition where both the NmC and Hib are conjugated to OMVs and therefore would not be rendered obvious by the proposed combination of references.

The Office has also not demonstrated how Vella *et al.* or Frasch could provide a reasonable expectation of success where the other art cited has not.

For at least the reasons set forth above, Applicants assert that claims 18 and 19 would not be obvious in view of Granoff *et al.*, 1997, Granoff *et al.*, 1992, Vella *et al.*, and Frasch. Therefore, Applicants respectfully request that the rejection under 35 U.S.C. § 103(a) be withdrawn.

Claim 21

Claim 21 is rejected under § 103(a) as allegedly being unpatentable over Granoff *et al.*, 1997 as modified by Granoff *et al.*, 1992, Vella *et al.*, Frasch, and further in view of Dalseg *et al.* (In: Vaccines 96. (Ed) Brown F. Cold Spring harbor Laboratory Press, Cold Spring Harbor, N.Y., pages 177-182, 1996, of record).

Applicants respectfully traverse the rejection and its supporting remarks. As discussed above, the Examiner has not established a *prima facie* case of obviousness as there is no reasonable expectation of success for the particular combination of Granoff *et al.*, 1997 and Granoff *et al.*, 1992. The Office has not demonstrated how Dalseg *et al.* could provide a reasonable expectation of success where the other art cited has not. Applicants therefore respectfully request that this rejection under 35 U.S.C. § 103(a) be withdrawn.

Claim 24

Claim 24 is rejected under § 103(a) as allegedly being unpatentable over Granoff *et al.*, 1997 as modified by Granoff *et al.*, 1992, Vella *et al.*, Frasch, and further in view of Seid (US 6,638,513, of record) ('513) or Granoff (WO 98/58670) ('670).

Applicants respectfully traverse the rejection and its supporting remarks. As discussed above, the Examiner has not established a *prima facie* case of obviousness as there is no reasonable expectation of success for the particular combination of Granoff *et al.*, 1997 and Granoff *et al.*, 1992. The Office has not demonstrated how Seid ('513) or Granoff ('670) could provide a

reasonable expectation of success where the other art cited has not. Applicants therefore respectfully request that this rejection under 35 U.S.C. § 103(a) be withdrawn.

VI. Objection to the Claims and Allowable Claims

The Office has objected to claim 20 as being dependent upon a rejected base claim, but found that the claim would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. For the reasons stated above, Applicants respectfully assert that the objected claim depends from an allowable claim. Applicants therefore respectfully request that this basis for objection be withdrawn.

CONCLUSION

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 223002100100. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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